--123. (Amended) A composition of matter comprising the antibody of any one of claims [114-121] 114-118 or 120-121 and an agent conjugated to the antibody.--

REMARKS

Initially applicants would like to thank the Examiner for the courtesy extended during the interview held on November 21, 2000 and attended by John P. White, Spencer Schneider, S. Leslie Misrock, Paul Maddon, Edward Gates and William Goeckler. Applicants believe this interview was most helpful in advancing prosecution of this application and that based on the amendments set forth above, applicants understand that the claims are likely in condition for allowance subject to the possible declaration of an interference with Bander, U.S. Patent No. 6,107,090 as discussed further below.

Claims 114-126 are pending in the subject application. Applicants have hereinabove canceled claim 119 without disclaimer or prejudice to applicant's right to pursue the subject matter of this claim in a later-filed application. Applicants have also amended claims 114-118 and 120-123. Support for these amendments may be found inter alia in the specification as follows: claims 114-116: page 55, lines 5-10; claims 117-118: page 55, lines 5-10 and Figure 14-1; and claims 120-121: page 22, lines 10-11 and page 53, lines 20-24. These amendments do not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 114-118 and 120-126 will be pending.

Rejection under 35 U.S.C. 112, first paragraph

In the May 24, 2000 Office Action, the Examiner rejected claim 126 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner stated that the method claim is not enabled because the specification does not provide an adequate written description, examples, or guidance for the following reasons. The Examiner stated that the antibodies used to perform the method are raised against antigens that are present in normal as well as cancerous prostate cells (citing Horoszewicz, US 5,162,504, abstract and claim 1). The Examiner stated that because the antigens are found in normal cells, the antibody would bind to normal cells, and the artisan would not have a predictable, reasonable expectation of success for using the instant invention to image prostate cancer because the composition of matter being used (the antibody), cannot distinguish cancer cells from normal cells, i.e. the antibody would bind to both normal and abnormal cells.

In response, applicants respectfully traverse the Examiner's rejection. As discussed during the interview, although prostate specific membrane antigen may be expressed on both normal and malignant prostate epithelial cells, its expression is significantly enhanced on malignant cells. In support, applicants attach hereto as **Exhibit A** a copy of Wright et al. (1995) entitled "Expression of Prostate-Specific Membrane Antigen in Normal, Benign, and Malignant Prostate Tissues" Urol. Oncol 1:18-28. On page 27, in column 1 Wright et al. state that this "study demonstrates the **differential expression** of PSMA in normal, benign and malignant prostate tissues" [emphasis added]. The paper also states that "PSMA was **overexpressed** in the poorly differentiated and metastatic tumors" [emphasis added]. In further support of this fact, applicants attach hereto as **Exhibit B** a copy of Sweat et al. (1998) entitled "Prostate-Specific Membrane Antigen Expression is Greatest in Prostate Adenocarcinoma and Lymph Node Metastes"

Urology 52(4):637-640. On page 640, in column 1 Sweat et al. state "we found consistent PSMA immunoreactivity in benign epithelium, primary prostate cancer, and lymph node metastases, with expression highest in cancer and lymph node metastases." These papers establish that there is differential expression of PSMA in normal and cancer cells. Moreover, as was pointed out during the interview, the 7E11-C5 monoclonal antibody is FDA approved for use in imaging, further evidencing the enablement of claims 126. Therefore, the invention recited in claim 126 is enabled because one skilled in the art would be able to image prostate cancer using the claimed method without undue experimentation and with a reasonable certainty of success. Applicants contend that these remarks obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. §102(e)

In the May 24, 2000 Office Action, the Examiner also rejected claims 119-126 under 35 U.S.C. §102(e) as anticipated by Horoszewicz. The Examiner stated that Horoszewicz discloses 7E11-C5, a monoclonal antibody that binds to PSMA (column 11, lines 27-56 and column 12, lines 31, line 12) which meet all the limitations of the instant claims because of the inherency of SEQ ID NO:2 to PSMA. In addition, the open language of claim 121 and the recitation of the outside region is anticipated by Horoszewicz.

In response, applicants respectfully traverse the Examiner's above rejection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claim 119 without prejudice to applicants' right to pursue the subject matter of this claim in a later-filed application and have amended claims 114-118 and 120-121. The Examiner is rejecting the claims based on

the disclosure of Horoszewicz, which discloses the 7E11-C5 antibody. As demonstrated in Figure 2 of Horoszewicz, the 7E11-C5 antibody binds to the inner or cytoplasmic region of the PSMA antigen. In contrast, the new pending claims recite an "antibody which binds to an **outside region** of prostate specific membrane antigen" [emphasis added]. Accordingly, Horoszewicz does not anticipate nor would it render obvious the claimed invention. Applicants contend that these amendments and remarks obviate this ground of rejection and respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §102(e).

Rejection under 35 U.S.C. §102(b)

In the May 24, 2000 Office Action, the Examiner also rejected claims 119-122 under 35 U.S.C. §102(b) as anticipated by Feng et al. 1991. The Examiner stated that Feng et al discloses an isolated PSM antigen with a molecular weight of 100 kda and a monoclonal antibody (7E11-C5) which reacts with said antigen. The Examiner stated that applicant's arguments filed June 17, 1999 have been fully considered but they are not persuasive.

In response, applicants respectfully traverse the Examiner's above rejection. Nevertheless, applicants without conceding the correctness of the examiner's position but to expedite prosecution of the subject application have hereinabove canceled claim 119 without disclaimer or prejudice to applicants' right to pursue the subject matter of this claim in a later-filed application and have amended claims 114-118 and 120-123. Feng discloses the 7E11-C5 antibody. As stated supra on page 7, the 7E11-C5 antibody binds to the inner or cytoplasmic region of PSMA. In contrast, the now pending claims of the subject application recite an "antibody which binds to an **outside region** of prostate specific membrane antigen"

[emphasis added]. Accordingly, Feng does not anticipate nor render obvious the claimed invention. Applicants contend that this amendment obviates the above ground of rejection and respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §102(b).

In summary, for the reasons set forth applicants maintain that the claims now pending in this application are in condition for allowance subject to the issue of a possible interference discussed below.

Applicant's Request for Interference

Pursuant to 37 C.F.R. §1.607, applicants hereby request an interference with U.S. Patent No. 6,107, 090, issued August 22, 2000. A copy of this patent was submitted to the United States Patent Office in a Supplemental Information Disclosure Statement filed on October 20, 2000 in connection with the subject application. An additional copy of this patent is attached hereto as **Exhibit C**.

Claim 25 of U.S. Patent No. 6,107,090 recites as follows:

> An isolated antibody or antigen binding portion thereof which binds to an extracellular domain of prostate specific membrane antigen which binding occurs to living cells, wherein said antibody or antigen binding portion thereof is selected for its ability to bind to live cells.

Claim 120 (as amended hereinabove) recites as follows:

> An antibody which binds to a fragment of prostate

> specific membrane antigenic polypeptide, which polypeptide fragment corresponds to an outside region of prostate specific membrane antigen, the amino acid sequence of which antigen is set forth in SEQ ID NO:2.

Applicants hereby propose the following count for the interference

> An isolated antibody which binds to an extracellular domain of prostate specific membrane antigen which binding occurs to living cells, wherein said antibody is selected for its ability to bind to live cells, or an antibody which binds to a fragment of prostate specific membrane antigenic polypeptide which polypeptide fragment corresponds to an outside region of prostate specific membrane antigen, the amino acid sequence of which antigen is set forth in SEQ ID NO:2.

The proposed count is claim 25 of U.S. Patent No. 6,107,090 or claim 120 of the subject application. Therefore, at least claim 25 of the patent and claim 120 of the subject application correspond to the count.

In addition, all of the claims of U.S. Patent No. 6,107,090 in addition to claim 25 correspond to the count. In contrast, applicants' claims 114-118 and 121-126 do not correspond to the proposed count.

Pursuant to 37 C.F.R. §1.607(d) applicants specifically request that a notice be placed in the file of U.S. Patent No. 6,107,090 that applicants are seeking to provoke an interference with the patent and that a copy of the notice be sent to the patentee.

Finally, pursuant to 37 C.F.R. §1.608, no prima facie showing is

required by applicants since applicants' effective filing date is November 5, 1992 and the patent's earliest possible date is May 6, 1996. Therefore, applicants are also entitled to be designated the senior party in the interference.

Applicants are in compliance with 35 U.S.C. §135(b) since less than one year has elapsed since the issuance of U.S. Patent No. 6,107,090. Moreover, claims which recited "substantially the same subject matter" as those in the patent were pending in the subject application prior to the issuance of the patent.

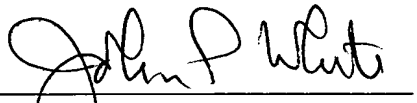
U.S. Serial No. 08/242,404

Pursuant to their duty of disclosure under 37 C.F.R. §1.56 and as discussed in the interview, applicants disclose the existence U.S. Serial No. 08/242,404, filed May 13, 1994, licensed to Cytogen Corp, which is also the licensee of the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invites the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $445.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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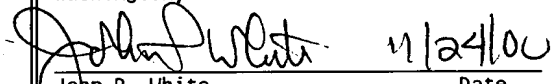
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.



11/24/00

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